IN THE SPECIFICATION

At page 1, line 28 through page 2, line 3, please replace the paragraph with the following text:

In contrast to the salvage pathway, uridine kinase is not normally involved in the biosynthesis pathway of UMP. Such a biosynthesis pathway utilizes carbamoyl phosphate, which is synthesized from glutamine catalyzed by carbamoyl phosphate synthetase II (CPS-II). Carbamoyl phosphate is then converted to UMP via the intermediates orotic acid and orotate monophosphate (OMP), and can be further processed to make other nucleotides. UMP is involved in feedback regulation of CPS-II to attenuate orotic acid production. (King, Michael W. (1998) ~~http://~~www.med.monash.edu.au/biochem/thcme/nucmetab.html).

At page 2, lines 11-19, please replace the paragraph with the following text:

The major function of pyrimidine nucleotide kinases, such as uridine kinase, is to maintain cellular balance between the level of pyrimidine nucleosides such as uridine and pyrimidine nucleoside monophosphates, in this case UMP. (King, Michael W. (1998) ~~http://~~www.med.monash.edu.au/biochem/thcme/nucmetab.html.) Uridine kinase activity is present in a variety of bacteria and animal cells, including tumors, and is especially high in cells of high growth rate. (Zubay, Geoffrey (1984) *Biochemistry* 712.) Uridine kinase has also been considered to be important in chemotherapy because uridine kinase has been shown to be required for the intracellular transformation of some pyrimidine nucleoside analogs to cytotoxic nucleotides. (Ropp, *supra.*)

At page 3, lines 1-15, please replace the paragraph with the following text:

Accordingly, in one aspect, the invention features a nucleic acid molecule which encodes a 57658 protein or polypeptide, e.g., a biologically active portion of the 57658 protein. In a preferred embodiment, the isolated nucleic acid molecule encodes a polypeptide having the amino acid sequence of SEQ ID NO:2. In other embodiments, the invention provides an isolated 57658 nucleic acid molecule having the nucleotide sequence shown in SEQ ID NO:1 or SEQ ID NO:3~~SEQ ID NO:1, SEQ ID NO:3, or the sequence of the DNA insert of the plasmid deposited with ATCC Accession Number ____~~. In still other embodiments, the invention provides nucleic acid molecules that are substantially identical (e.g., naturally occurring allelic variants) to the nucleotide sequence shown in SEQ ID NO:1 or SEQ ID

NO:3~~SEQ ID NO:1, SEQ ID NO:3, or the sequence of the DNA insert of the plasmid deposited with ATCC Accession Number ____~~. In other embodiments, the invention provides a nucleic acid molecule which hybridizes under stringent hybridization conditions to a nucleic acid molecule comprising the nucleotide sequence of SEQ ID NO:1 or SEQ ID NO:3~~SEQ ID NO:1, SEQ ID NO:3, or the sequence of the DNA insert of the plasmid deposited with ATCC Accession Number ____~~, wherein the nucleic acid encodes a full length 57658 protein or an active fragment thereof.

At page 4, lines 1-10, please replace the paragraph with the following text:

In other embodiments, the invention provides 57658 polypeptides, e.g., a 57658 polypeptide having the amino acid sequence shown in SEQ ID NO:2~~; the amino acid sequence encoded by the cDNA insert of the plasmid deposited with ATCC Accession Number ____~~; an amino acid sequence that is substantially identical to the amino acid sequence shown in SEQ ID NO:2; or an amino acid sequence encoded by a nucleic acid molecule having a nucleotide sequence which hybridizes under stringent hybridization conditions to a nucleic acid molecule comprising the nucleotide sequence of SEQ ID NO:1 or SEQ ID NO:3~~SEQ ID NO:1, SEQ ID NO:3, or the sequence of the DNA insert of the plasmid deposited with ATCC Accession Number ____~~, wherein the nucleic acid encodes a full length 57658 protein or an active fragment thereof.

At page 5, line 21, through page 6, line 5, please replace the paragraphs with the following text:

Figure 4 depicts a BLAST alignment of human 57658 with a consensus amino acid sequence derived from a ProDomain "kinase uridine monophophokinase transferase ATP-binding kinase-like ribonucleoside pyrimidine FIS cDNA" (Release 2001.1; ~~http:~~//www.toulouse.inra.fr/prodom.html). The lower sequence is amino acid residues 1 to 125 of the 125 amino acid consensus sequence (SEQ ID NO:5), while the upper amino acid sequence corresponds to the "kinase uridine monophophokinase transferase ATP-binding kinase-like ribonucleoside pyrimidine FIS cDNA" domain of human 57658, amino acid residues 154 to 277 of SEQ ID NO:2.

Figure 5 depicts a BLAST alignment of human 57658 with a consensus amino acid sequence derived from a ProDomain "kinase uridine transferase ATP-binding phosphoribulokinase monophophokinase precursor PRK cycle phosphopentokinase" (Release 2001.1; ~~http:~~//www.toulouse.inra.fr/prodom.html). The lower sequence is amino acid residues 4 to 127 of the amino acid consensus sequence (SEQ ID NO:6), while the upper amino acid sequence corresponds to the

"kinase uridine transferase ATP-binding phosphoribulokinase monophophokinase precursor PRK cycle phosphopentokinase" domain of human 57658, amino acid residues 25 to 151 of SEQ ID NO:2.

At page 8, lines 21-24, please replace the paragraph with the following text:

Human 57658 contains the following regions or other structural features (for general information regarding PFAM identifiers, PS prefix and PF prefix domain identification numbers, refer to Sonnhammer et al. (1997) Protein 28:405-420 and ~~http://~~www.psc.edu/general/software/packages/pfam/pfam.html):

At page 9, lines 18-27, please replace the paragraphs with the following text:

For general information regarding PFAM identifiers, PS prefix and PF prefix domain identification numbers, refer to Sonnhammer et al. (1997) *Protein* 28:405-420 and ~~http//~~www.psc.edu/general/software/packages/pfam/pfam.html.

~~A plasmid containing the nucleotide sequence encoding human 57658 was deposited with American Type Culture Collection (ATCC), 10801 University Boulevard, Manassas, VA 20110-2209, on _____ and assigned Accession Number _____. This deposit will be maintained under the terms of the Budapest Treaty on the International Recognition of the Deposit of Microorganisms for the Purposes of Patent Procedure. This deposit was made merely as a convenience for those of skill in the art and is not an admission that a deposit is required under 35 U.S.C. §112.~~

At page 11, lines 16-29, please replace the paragraph with the following text:

To identify the presence of a "uridine kinase" domain in a 57658 protein sequence, and make the determination that a polypeptide or protein of interest has a particular profile, the amino acid sequence of the protein can be searched against a database of HMMs (e.g., the Pfam database, release 2.1) using the default parameters (~~http://~~www.sanger.ac.uk/Software/Pfam/HMM search). For example, the hmmsf program, which is available as part of the HMMER package of search programs, is a family specific default program for MILPAT0063 and a score of 15 is the default threshold score for determining a hit. Alternatively, the threshold score for determining a hit can be lowered (e.g., to 8 bits). A description of the Pfam database can be found in Sonhammer et al., (1997) *Proteins* 28(3):405-420 and a detailed

description of HMMs can be found, for example, in Gribskov et al., (1990) *Meth. Enzymol.* 183:146-159; Gribskov et al., (1987) *Proc. Natl. Acad. Sci. USA* 84:4355-4358; Krogh et al., (1994) *J. Mol. Biol.* 235:1501-1531; and Stultz et al., (1993) *Protein Sci.* 2:305-314, the contents of which are incorporated herein by reference.

At page 12 lines 1-10, please replace the paragraph with the following text:

To identify the presence of a relevant domain in a 57658 protein sequence, and make the determination that a polypeptide or protein of interest has a particular profile, the amino acid sequence of the protein can be searched against a SMART database (Simple Modular Architecture Research Tool, ~~http://~~smart.embl-heidelberg.de/) of HMMs as described in Schultz et al. (1998), *Proc. Natl. Acad. Sci.* USA 95:5857 and Schultz et al. (2000) Nucl. Acids Res 28:231. The database contains domains identified by profiling with the hidden Markov models of the HMMer2 search program (R. Durbin et al. (1998) *Biological sequence analysis: probabilistic models of proteins and nucleic acids.* Cambridge University Press.; ~~http://~~hmmer.wustl.edu/). The database also is extensively annotated and monitored by experts to enhance accuracy.

At page 20, lines 1-25, please replace the paragraphs with the following text:

A "non-essential" amino acid residue is a residue that can be altered from the wild-type sequence of 57658(e.g., the sequence of SEQ ID NO:1 or SEQ ID NO:3~~SEQ ID NO:1, SEQ ID NO:3, or the nucleotide sequence of the DNA insert of the plasmid deposited with ATCC as Accession Number ——~~) without abolishing or more preferably, without substantially altering a biological activity, whereas an "essential" amino acid residue results in such a change. For example, amino acid residues that are conserved among the polypeptides of the present invention, e.g., those present in the uridine kinase domain, are predicted to be particularly unamenable to alteration.

A "conservative amino acid substitution" is one in which the amino acid residue is replaced with an amino acid residue having a similar side chain. Families of amino acid residues having similar side chains have been defined in the art. These families include amino acids with basic side chains (e.g., lysine, arginine, histidine), acidic side chains (e.g., aspartic acid, glutamic acid), uncharged polar side chains (e.g., glycine, asparagine, glutamine, serine, threonine, tyrosine, cysteine), nonpolar side chains (e.g., alanine, valine, leucine, isoleucine, proline, phenylalanine, methionine, tryptophan), beta-branched side chains (e.g., threonine, valine, isoleucine) and aromatic side chains (e.g., tyrosine, phenylalanine,

tryptophan, histidine). Thus, a predicted nonessential amino acid residue in a 57658 protein is preferably replaced with another amino acid residue from the same side chain family. Alternatively, in another embodiment, mutations can be introduced randomly along all or part of a 57658 coding sequence, such as by saturation mutagenesis, and the resultant mutants can be screened for 57658 biological activity to identify mutants that retain activity. Following mutagenesis of SEQ ID NO:1 or SEQ ID NO:3~~SEQ ID NO:1, SEQ ID NO:3, or the nucleotide sequence of the DNA insert of the plasmid deposited with ATCC as Accession Number _____~~, the encoded protein can be expressed recombinantly and the activity of the protein can be determined.

At page 21, line 28 through page 22, line 10, please replace the paragraph with the following text:

The comparison of sequences and determination of percent identity between two sequences can be accomplished using a mathematical algorithm. In a preferred embodiment, the percent identity between two amino acid sequences is determined using the Needleman and Wunsch (*J. Mol. Biol.* (48):444-453 (1970)) algorithm which has been incorporated into the GAP program in the GCG software package (available at ~~http://~~www.gcg.com), using either a Blossum 62 matrix or a PAM250 matrix, and a gap weight of 16, 14, 12, 10, 8, 6, or 4 and a length weight of 1, 2, 3, 4, 5, or 6. In yet another preferred embodiment, the percent identity between two nucleotide sequences is determined using the GAP program in the GCG software package (available at ~~http://~~www.gcg.com), using a NWSgapdna.CMP matrix and a gap weight of 40, 50, 60, 70, or 80 and a length weight of 1, 2, 3, 4, 5, or 6. A particularly preferred set of parameters (and the one that should be used if the practitioner is uncertain about what parameters should be applied to determine if a molecule is within a sequence identity or homology limitation of the invention) is using a Blossum 62 scoring matrix with a gap open penalty of 12, a gap extend penalty of 4, and a frameshift gap penalty of 5.

At page 22, lines 15-27, please replace the paragraph with the following text:

The nucleic acid and protein sequences described herein can be used as a "query sequence" to perform a search against public databases to, for example, identify other family members or related sequences. Such searches can be performed using the NBLAST and XBLAST programs (version 2.0) of Altschul, et al., (1990) *J. Mol. Biol.* 215:403-10. BLAST nucleotide searches can be performed with the NBLAST program, score = 100, wordlength = 12 to obtain nucleotide sequences homologous to 57658 nucleic acid molecules of the invention. BLAST protein searches can be performed with the XBLAST

program, score = 50, wordlength = 3 to obtain amino acid sequences homologous to 57658 protein molecules of the invention. To obtain gapped alignments for comparison purposes, Gapped BLAST can be utilized as described in Altschul et al., (1997) *Nucleic Acids Res.* 25(17):3389-3402. When utilizing BLAST and Gapped BLAST programs, the default parameters of the respective programs (e.g., XBLAST and NBLAST) can be used. See ~~http://~~www.ncbi.nlm.nih.gov.

At page 23, line 27 through page 24, line 27, please replace the paragraphs with the following text:

In one embodiment, an isolated nucleic acid molecule of the invention includes the nucleotide sequence shown in SEQ ID NO:1~~, or the nucleotide sequence of the DNA insert of the plasmid deposited with ATCC as Accession Number _____~~, or a portion of any of these nucleotide sequences. In one embodiment, the nucleic acid molecule includes sequences encoding the human 57658 protein (i.e., "the coding region", from nucleotides 1-834 of SEQ ID NO:1, not including the terminal codon), as well as 5' untranslated sequences (93 nucleotides before the coding region of SEQ ID NO:1). Alternatively, the nucleic acid molecule can include only the coding region of SEQ ID NO:1 (e.g., nucleotides 1-834 of SEQ ID NO:1, corresponding to SEQ ID NO:3) and, e.g., no flanking sequences which normally accompany the subject sequence. In another embodiment, the nucleic acid molecule encodes a sequence corresponding to the mature protein of SEQ ID NO:2.

In another embodiment, an isolated nucleic acid molecule of the invention includes a nucleic acid molecule which is a complement of the nucleotide sequence shown in SEQ ID NO:1 or SEQ ID NO:3~~SEQ ID NO:1, SEQ ID NO:3, or the nucleotide sequence of the DNA insert of the plasmid deposited with ATCC as Accession Number _____~~, or a portion of any of these nucleotide sequences. In other embodiments, the nucleic acid molecule of the invention is sufficiently complementary to the nucleotide sequence shown in SEQ ID NO:1 or SEQ ID NO:3~~SEQ ID NO:1, SEQ ID NO:3, or the nucleotide sequence of the DNA insert of the plasmid deposited with ATCC as Accession Number _____~~ such that it can hybridize to the nucleotide sequence shown in SEQ ID NO:1 or SEQ ID NO:3~~SEQ ID NO:1, SEQ ID NO:3, or the nucleotide sequence of the DNA insert of the plasmid deposited with ATCC as Accession Number _____~~, thereby forming a stable duplex.

In one embodiment, an isolated nucleic acid molecule of the present invention includes a nucleotide sequence which is at least about 60%, 65%, 70%, 75%, 80%, 85%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or more homologous to the nucleotide sequence shown in SEQ ID NO:1 or SEQ ID NO:3~~SEQ ID NO:1, SEQ ID NO:3, or the nucleotide sequence of the DNA insert of the plasmid deposited with ATCC as Accession Number _____~~. In the case of an isolated nucleic acid molecule which is longer than or equivalent in length to the reference sequence, e.g., SEQ ID NO:1, or

SEQ ID NO:3, the comparison is made with the full length of the reference sequence. Where the isolated nucleic acid molecule is shorter than the reference sequence, e.g., shorter than SEQ ID NO:1, or SEQ ID NO:3, the comparison is made to a segment of the reference sequence of the same length (excluding any loop required by the homology calculation).

At page 24, line 30 through page 25, line 8, please replace the paragraph with the following text:

A nucleic acid molecule of the invention can include only a portion of the nucleic acid sequence of SEQ ID NO:1 or SEQ ID NO:3~~SEQ ID NO:1, SEQ ID NO:3, or the nucleotide sequence of the DNA insert of the plasmid deposited with ATCC as Accession Number _____~~. For example, such a nucleic acid molecule can include a fragment which can be used as a probe or primer or a fragment encoding a portion of a 57658 protein, e.g., an immunogenic or biologically active portion of a 57658 protein. A fragment can comprise: nucleotides of SEQ ID NO:1, which encodes a kinase or specifically, a uridine kinase domain of human 57658. The nucleotide sequence determined from the cloning of the 57658 gene allows for the generation of probes and primers designed for use in identifying and/or cloning other 57658 family members, or fragments thereof, as well as 57658 homologues, or fragments thereof, from other species.

At page 25, lines 23-31, please replace the paragraph with the following text:

57658 probes and primers are provided. Typically a probe/primer is an isolated or purified oligonucleotide. The oligonucleotide typically includes a region of nucleotide sequence that hybridizes under stringent conditions to at least about 7, 12 or 15, preferably about 20 or 25, more preferably about 30, 35, 40, 45, 50, 55, 60, 65, or 75 consecutive nucleotides of a sense or antisense sequence of SEQ ID NO:1 or SEQ ID NO:3~~SEQ ID NO:1, SEQ ID NO:3, or the nucleotide sequence of the DNA insert of the plasmid deposited with ATCC as Accession Number _____~~, or of a naturally occurring allelic variant or mutant of SEQ ID NO:1 or SEQ ID NO:3~~SEQ ID NO:1, SEQ ID NO:3, or the nucleotide sequence of the DNA insert of the plasmid deposited with ATCC as Accession Number _____~~.

At page 26, line 18 through page 27, line 15, please replace the paragraphs with the following text:

A nucleic acid fragment encoding a "biologically active portion of a 57658 polypeptide" can be prepared by isolating a portion of the nucleotide sequence of SEQ ID NO:1 or SEQ ID NO:3~~SEQ ID NO:1, SEQ ID NO:3, or the nucleotide sequence of the DNA insert of the plasmid deposited with ATCC as Accession Number _____~~, which encodes a polypeptide having a 57658 biological activity (e.g., the biological activities of the 57658 proteins as described herein), expressing the encoded portion of the 57658 protein (e.g., by recombinant expression *in vitro*) and assessing the activity of the encoded portion of the 57658 protein. For example, a nucleic acid fragment encoding a biologically active portion of 57658 includes a uridine kinase domain. A nucleic acid fragment encoding a biologically active portion of a 57658 polypeptide, may comprise a nucleotide sequence which is greater than 300-1200 or more nucleotides in length.

In preferred embodiments, nucleic acids include a nucleotide sequence which is about 300, 400, 500, 600, 700, 800, 900, 1000, 1100, 1200, 1300, 1400 nucleotides in length and hybridizes under stringent hybridization conditions to a nucleic acid molecule of SEQ ID NO:1, or SEQ ID NO:3~~, or the nucleotide sequence of the DNA insert of the plasmid deposited with ATCC as Accession Number _____~~.

57658 Nucleic Acid Variants

The invention further encompasses nucleic acid molecules that differ from the nucleotide sequence shown in SEQ ID NO:1 or SEQ ID NO:3~~SEQ ID NO:1, SEQ ID NO:3, or the nucleotide sequence of the DNA insert of the plasmid deposited with ATCC as Accession Number _____~~. Such differences can be due to degeneracy of the genetic code (and result in a nucleic acid which encodes the same 57658 proteins as those encoded by the nucleotide sequence disclosed herein. In another embodiment, an isolated nucleic acid molecule of the invention has a nucleotide sequence encoding a protein having an amino acid sequence which differs, by at least 1, but less than 5, 10, 20, 50, or 100 amino acid residues that shown in SEQ ID NO:2. If alignment is needed for this comparison the sequences should be aligned for maximum homology. "Looped" out sequences from deletions or insertions, or mismatches, are considered differences.

At page 27, line 27 through page 28, line 2, please replace the paragraph with the following text:

In a preferred embodiment, the nucleic acid differs from that of SEQ ID NO:1 or SEQ ID NO:3~~SEQ ID NO:1, SEQ ID NO:3, or the nucleotide sequence of the DNA insert of the plasmid deposited with ATCC as Accession Number _____~~, e.g., as follows: by at least one but less than 10, 20, 30, or 40 nucleotides; at least one but less than 1%, 5%, 10% or 20% of the in the subject nucleic acid. If necessary for

this analysis the sequences should be aligned for maximum homology. "Looped" out sequences from deletions or insertions, or mismatches, are considered differences.

At page 28, lines 25-28, please replace the paragraph with the following text:

Moreover, nucleic acid molecules encoding other 57658 family members and, thus, which have a nucleotide sequence which differs from the 57658 sequences of SEQ ID NO:1 or SEQ ID NO:3~~SEQ ID NO:1, SEQ ID NO:3, or the nucleotide sequence of the DNA insert of the plasmid deposited with ATCC as Accession Number _____~~ are intended to be within the scope of the invention.

At page 36, line 28 through page 37, line 7, please replace the paragraphs with the following text:

In another aspect, the invention features a method of making a fragment or analog of a 57658 polypeptide a biological activity of a naturally occurring 57658 polypeptide. The method includes: altering the sequence, e.g., by substitution or deletion of one or more residues, of a 57658 polypeptide, e.g., altering the sequence of a non-conserved region, or a domain or residue described herein, and testing the altered polypeptide for the desired activity.

[[¶]]

[[¶]]

[[¶]]

[[¶]]

[[¶]]

Anti-57658 Antibodies

In another aspect, the invention provides an anti-57658 antibody. The term "antibody" as used herein refers to an immunoglobulin molecule or immunologically active portion thereof, i.e., an antigen-binding portion. Examples of immunologically active portions of immunoglobulin molecules include F(ab) and $F(ab')_2$ fragments which can be generated by treating the antibody with an enzyme such as pepsin.

At page 60, lines 15-24, please replace the paragraph with the following text:

The isolated mRNA can be used in hybridization or amplification assays that include, but are not limited to, Southern or Northern analyses, polymerase chain reaction analyses and probe arrays. One preferred diagnostic method for the detection of mRNA levels involves contacting the isolated mRNA with a nucleic acid molecule (probe) that can hybridize to the mRNA encoded by the gene being detected. The nucleic acid probe can be, for example, a full-length 57658 nucleic acid, such as the nucleic acid of SEQ ID NO:1~~, or the DNA insert of the plasmid deposited with ATCC as Accession Number _____~~, or a portion thereof, such as an oligonucleotide of at least 7, 15, 30, 50, 100, 250 or 500 nucleotides in length and sufficient to specifically hybridize under stringent conditions to 57658 mRNA or genomic DNA. Other suitable probes for use in the diagnostic assays are described herein.